PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 718346C:ANB:VNB	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. **PCT**/AU2005/000041	International filing date *(day/month/year)* 14 January 2005	Priority date *(day/month/year)* 16 January 2004
International Patent Classification (IPC) or national classification and IPC Int. Cl. ***A61K 38/16*** (2006.01) ***A61P 37/02*** (2006.01)		
Applicant BRISBANE TECHNOLOGY PARK et al		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. [X] *(sent to the applicant and to the International Bureau)* a total of **1** sheets, as follows:
      - [ ] sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      - [ ] sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.

   b. [ ] *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or table related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items:
   - [X] Box No. I Basis of the report
   - [ ] Box No. II Priority
   - [ ] Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - [ ] Box No. IV Lack of unity of invention
   - [X] Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - [X] Box No. VI Certain documents cited
   - [ ] Box No. VII Certain defects in the international application
   - [ ] Box No. VIII Certain observations on the international application

Date of submission of the demand 15 November 2005	Date of completion of this report 24 May 2006
Name and mailing address of the IPEA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	Authorized Officer **GARETH COOK** Telephone No. (02) 6283 2541

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/AU2005/000041

Box No. I Basis of the report

1. With regard to the **language**, this report is based on:

[X] The international application in the language in which it was filed

[ ] A translation of the international application into , which is the language of a translation furnished for the purposes of:

[ ] international search (under Rules 12.3(a) and 23.1 (b))

[ ] publication of the international application (under Rule 12.4(a))

[ ] international preliminary examination (Rules 55.2(a) and/or 55.3(a))

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

[ ] the international application as originally filed/furnished

[X] the description:

pages **1-49** as originally filed/furnished
pages* received by this Authority on with the letter of
pages* received by this Authority on with the letter of

[ ] the claims:

pages **51-53** as originally filed/furnished
pages* as amended (together with any statement) under Article 19
pages* **50** received by this Authority on **15 November 2005** with the letter of 14 November 2004
pages* received by this Authority on with the letter of

[ ] the drawings:

pages as originally filed/furnished
pages* received by this Authority on with the letter of
pages* received by this Authority on with the letter of

[ ] a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. [ ] The amendments have resulted in the cancellation of:

[ ] the description, pages
[ ] the claims, Nos.
[ ] the drawings, sheets/figs
[ ] the sequence listing *(specify)*:
[ ] any table(s) related to the sequence listing *(specify)*:

4. [ ] This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

[ ] the description, pages
[ ] the claims, Nos.
[ ] the drawings, sheets/figs
[ ] the sequence listing *(specify)*:
[ ] any table(s) related to the sequence listing *(specify)*:

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

Box No. V **Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	**1-6, 30-39**	**YES**
	Claims	**7-29**	**NO**
Inventive step (IS)	Claims	**1-6, 30-39**	**YES**
	Claims	**7-29**	**NO**
Industrial applicability (IA)	Claims	**1-39**	**YES**
	Claims		**NO**

2. Citations and explanations (Rule 70.7)

The following documents identified in the International Search Report have been considered for the purposes of this report:

D1 Ragno S *et al*, *Clinical and Experimental Immunology*, 1996, 103:384-390
D2 Zhang B *et al*, *Journal of Neurological Sciences*, 2000, 182:5-15
D3 Zhang B *et al*, *Journal of Neurological Sciences*, 2003, 212:37-46

Novelty (N) and Inventive Step (IS) claims 7 to 29

D1 discloses an adjuvant arthritis model induced by heat killed strains of Mycobacterium tuberculosis. D2 and D3 disclose an autoimmune encephalomyelitis model induced by the lipoprotein myelin proteolipid protein. Each document discloses that treatment with Cpn10 (Hsp10, Early Pregnancy Factor) suppresses an autoimmune or inflammatory response or improves a humoral response. This is done in the presence of compounds used to replicate the disease state which the current application identifies as agonists of Toll Like Receptors (TLRs). It is therefore inherent that the mechanism through which Cpn10 is working involves the TLRs. Claims 7 to 29 are to methods of treatment involving the use of Cpn10. Discovering the mechanism through which Cpn10 works does not make does not make a claims to the use of Cpn10 to achieve a known result novel or inventive. It is an inherent step that occurs in the prior art methods, even though this inherent step was not known to be occurring. Claims 7 to 29 are not novel and do not involve an inventive step.

With respect to claims 20 to 29, the Attorney has submitted that these are claims to treating a disease, disorder or condition "responsive to regulation of toll-like receptor signalling" or "responsive to toll-like receptor induced immunomodulator production and/or secretion". The diseases, disorders and conditions included are given in 21 and 25. These are diseases, disorders or conditions shown in the prior art to be responsive to Cpn10. Merely putting into the claim the mechanism by which the treatment works does not make the method novel, as it is an inherent part of the method.

It has also been put forward by the Attorney that there could be any number of inflammatory pathways through which Cpn10 could be working, and this may not necessarily be through the toll-like receptors. The current application hypothesises that Cpn10 is working through the toll-like receptor for the various diseases, disorders or conditions, such as on pages 2 and 3. Assuming the specification is correct in its hypothesis, then it is inherent that Cpn10 is acting through the toll-like receptor in the prior art, the alternative being that what is stated in the specification is incorrect.

Continued in supplemental box.

Box No. VI Certain documents cited

1. Certain published documents (Rule 70.10)

Application No. Patent No.	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date (valid claim) *(day/month/year)*
WO 2004/041300	21 May 2004	6 November 2003	6 November 2002
WO 2004/041304	21 May 2004	5 November 2003	8 November 2002

WO 2004/041300 discloses that cpn10 treatment in response to stimulation by lipopolysaccharide increases IL10 production (page 29) and treatment by cpn10 in a model set up for LPS leakage through the gastro intestinal tract can delay graft versus host diseases (GVHD) and reduce TNFα production (pages 30 to 31).

WO 2004/041304 uses in the examples endotoxin to induce inflammatory hyperalgesia (page 10) and show that cpn10 has an analgesic effect (page 13).

While neither document makes reference to toll-like receptors, it is inherent that this is the pathway involved in the documents. Elucidating the mechanism by which a method works does not make the method itself novel. Claims 7 to 29 lack novelty when compared with these documents.

The comments made about the Attorney's submission in Box V also apply here.

2. Non-written disclosures (Rule 70.9)

Kind of non-written disclosure	Date of non-written disclosure *(day/month/year)*	Date of written disclosure referring to non-written disclosure *(day/month/year)*

Supplemental Box

In case **the space in any of the preceding boxes is not sufficient.**

Continuation of: Box V

Novelty (N) and Inventive Step (IS) claims 1 to 6 and 30 to 39

Claims 1 to 6 are to a "method of regulating Toll-like receptor signalling". The citations do not disclose the regulation of TLRs in the methods of treatment. Claims 1 to 6 are novel and involve an inventive step

The prior art does not disclose that Cpn10 interacts with TLRs, nor could this be predicted from the prior art. The claims to the complex, and to methods of compound design or screening involving interaction between cpn10 and TLRs are novel and inventive over the prior art.

Industrial Applicability (IA)

The invention defined in the claims is considered to meet the requirements of Industrial Applicability under Article 33(4) of the PCT because it can be made by, or used in, industry.

CLAIMS

1. A method of regulating Toll-like receptor signaling in an animal, or in one or more cells, or tissues or organs derived therefrom, including the step of administering Cpn10 to the animal, cells, tissues or organs, to thereby regulate agonist-induced Toll-like receptor signaling.

2. The method of Claim 1, wherein the Toll-like receptor is selected from the group consisting of TLR2 and TLR4.

3. The method of Claim 1, wherein the agonist is, or is derived from, a pathogen.

4. The method of Claim 3, wherein the agonist is selected from LPS, or lipopeptide.

5. The method of Claim 1, wherein the animal is a mammal.

6. The method of Claim 6, wherein the mammal is a human.

7. A method of regulating immunomodulator secretion in an animal, or in one or more cells, or tissues or organs derived therefrom, including the step of administering Cpn10, or a derivative of Cpn10, to the animal, cells, tissues or organs, to thereby regulate Toll-like receptor agonist-induced immunomodulator production and/or secretion.

8. The method of Claim 7, wherein the Toll-like receptor is selected from the group consisting of TLR2 and TLR4.

9. The method of Claim 7, wherein the agonist is, or is derived from, a pathogen.

10. The method of Claim 9, wherein the agonist is selected from LPS or a lipopeptide.

11. The method of Claim 7, wherein production and/or secretion of the immunomodulator is negatively regulated by Cpn10.

12. The method of Claim 11, wherein the immunomodulator is a pro-inflammatory cytokine or chemokine.

13. The method of Claim 12, wherein the pro-inflammatory cytokine is IL-6 or TNFα.

14. The method of Claim 12, wherein the pro-inflammatory chemokine is